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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,480	08/13/2002	Robert Heger	49619	4809

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EXAMINER
BENNETT, RACHEL M

ART UNIT	PAPER NUMBER
1615	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/857,480	Applicant(s) HEGER ET AL.	
	Examin r Rachel M. Bennett	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2001* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner acknowledges receipt of Preliminary Amendment A and IDS filed 6/5/01.

Specification

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1, 11, 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 13 recites the limitation ""the second viral coefficient" in line 1. There is insufficient antecedent basis for this limitation in the claim.

4. Claims 1 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 14 provides for the use of a preparation, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex*

parte Dunki, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 8-14 rejected under 35 U.S.C. 102(b) as being anticipated by Stainmesse (US 5133908).

Stainmesse et al disclose a process for the preparation of dispersible colloidal systems of a substance in the form of spherical particles of the matrix type and of a size less than 500 nm (nanoparticles), comprising: (1) the preparation of a liquid phase consisting essentially of a solution of the substance in a solvent or in a mixture of solvents to which may be added one or more surfactants, (2) the preparation of a second liquid phase consisting essentially of a non-solvent of a mixture of non-solvents for the substance and to which may be added one or more surfactants, the non-solvent or the mixture of non-solvents for the substance being miscible in all proportions with the solvent or the mixture of solvents for the substance, (3) the addition of one of the liquid phases prepared in (1) or (2) to the other with moderate stirring so as to produce a colloidal suspension of nanoparticles of the substance and, (4) if desired, the removal of all or part of the solvent or the mixture of solvents for the substance and of the non-solvent or the mixture of non-solvents for the substance so as to produce a colloidal suspension of

nanoparticles of the desired concentration or to produce a powder of nanoparticles. Said substance may be a protein. The nanoparticle may be used in chemistry, biochemistry, pharmacy, medicine, and cosmetics. In example 5, 5mg indomethacin and 125 mg D,L-polylactic acid are dissolved in 25 ml acetone. In order to produce the aqueous phase, 125 mg Poloxamer 188 are dissolved in 50 ml water. The acetone phase is stirred into the aqueous phase. Nanoparticles are obtained with an average diameter of 180 nm. After the acetone is evaporated under a reduced pressure, the remaining aqueous suspension can be further concentrated. Active substance resorption characteristics were examined using a series of tests on rats, to which and nanoparticle suspension was administered orally or intravenously. The production method described in Stainmesse corresponds to the method defined in Claim 11 of the instant application, in which D,L-polylactic acid represents the core polymer and Poloxamer 188 the sheathing polymer (see instant specification, page 5, lines 33-37, and page 4, lines 21-23). It could therefore also be assumed that the nanoparticles obtained according to Claim 1 and page 1, lines 7-11, of the instant application, have a core-shell structure in which the amorphous precipitated active substance is present in the core (compare with Example 14 of Stainmesse) in a matrix of D,L-polylactic acid, while the Poloxamer forms an external stabilizing layer. The nanoparticles meet the limitation of Claims 4 and 8. The aqueous nanoparticles suspension corresponds to the hydrosol instant claim 9. Therefore, these claims are anticipated.

8. Claims 1-6, 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by List et al. (US 5389382).

List discloses a hydrosol of a pharmacological active agent in an intravenous applicable, stabilized, pharmaceutically acceptable form, which form is suspended or is dry and re-

suspendable in an aqueous medium. The hydrosol contains solid active agent particles. See abstract. The hydrosol is started from a solution of a hardly water-soluble active substance in a water-miscible solvent. This solution is mixed with a relatively large amount of water containing a water-soluble colloid, for example gelatin. Alternatively or additionally, a water-insoluble colloid can be dissolved in the organic solvent. The colloid stabilized the active substance hydrosol formed when the phases are brought together. The organic solvent is then removed.

In Examples 4, 9 and 10, the pharmacologically active substance and ethyl cellulose re first dissolved in ethanol. The ethanolic phase is then stirred into an aqueous phase containing gelatin or a collagen hydrolysate. The ethanol is evaporated. The average particle diameter of the suspended particles is of 245 nm, 129nm, and 320 nm. The nanoparticles and their hydrosols correspond to the preparations defined in instant claims 1 and 9. Ethyl cellulose acts in this case as core polymer, the sheathing polymer is gelatin or collagen hydrolysate. Therefore, these claims are anticipated.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over List et al. (US 5389382).

List discloses a hydrosol of a pharmacological active agent in an intravenous applicable, stabilized, pharmaceutically acceptable form, which form is suspended or is dry and re-suspendable in an aqueous medium. List does not specifically disclose casein or sodium caseinate as a coating matrix.

Liversidge et al. discloses surface modified drug nanoparticles. Dispersible particles consisting essentially of a crystal-line drug substance having a surface modifer absorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less thatn about 400nm. Pharmaceutical compositions containing the particles exhibit unexpected bioavailablity and are useful in methods of treating mammals. See abstract. Suitable surface modifiers can preferably be selected from known excipients. Representative examples include gelatin, casein, lecithin, gum acacia, methylcellulose, etc. See col. 4 lines 34-64.

Absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of List by substituting casin as taught by Liversidge for gelatin as the coating polymer because of the expectation of exhibit unexpected bioavailablity and are useful in methods of treating mammals as taught by Liverside. Both gelatin and casein are known excipients used as surface modifiers. Therefore, substituting one for another would not require undue experimentation and one of ordinary skill in the art would expect similar results.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

R. Bennett
April 3, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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